

REMARKS

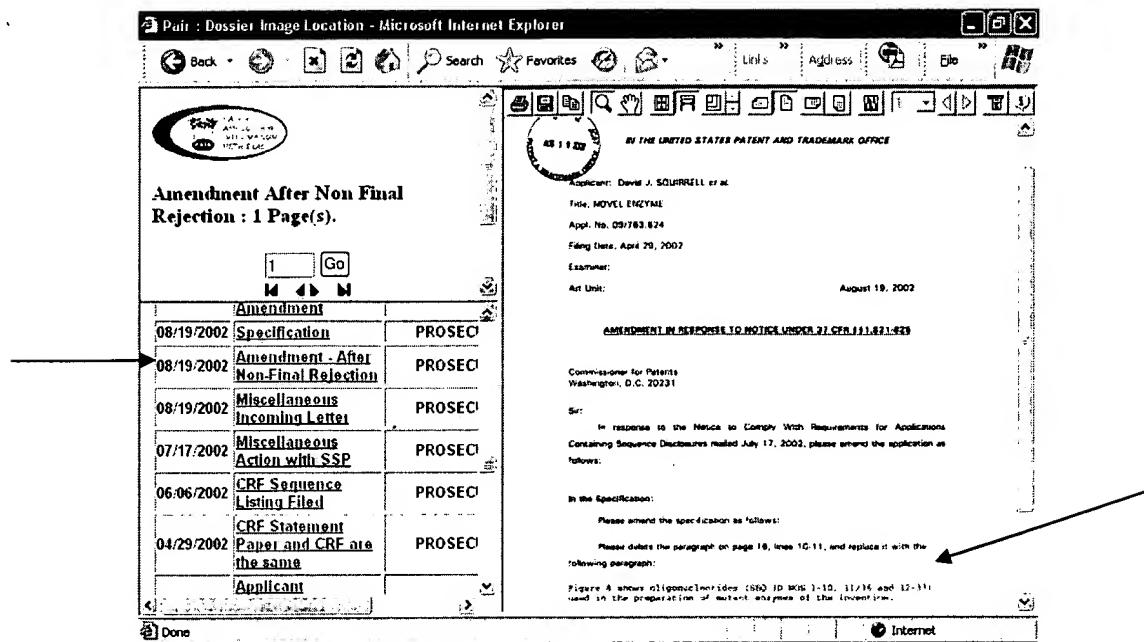
Reconsideration is requested.

Claims 1-66 have been canceled, without prejudice. Claims 67-85 have been added and are pending. No new matter has been added. Claims 67-85 are based on now-canceled claims 31-34, 37-38, 51-60 and 64-66.

The specification has been amended to include the attached revised Sequence Listing. The attached paper and computer readable copies of the Sequence Listing are the same. No new matter has been added. The Sequence Listing includes the *Photinus pyralis* wild-type luciferase amino acid sequence (designated SEQ ID NO: 37). The luciferase sequence of SEQ ID NO: 37 is obtainable from Ye et al. (1997; see *Ppy* sequence in Fig. 2 and reference to GenBank accession No. M15077 in Table 1), mentioned in the present application at page 7, lines 21-24. The luciferase sequence of SEQ ID NO: 37 is also obtainable from U.S. Patent No. 6,265,177B1 (see SEQ ID NO: 21) which is derived from International Patent Appl. No. PCT/GB98/01026 that is explicitly incorporated by reference in the present application at page 12, lines 14-15. No new matter has been added.

The Title has been revised as suggested by the Examiner. Withdrawal of the objection to the Title is requested.

The specification has been amended to correct the reference to Figure 8. The specification was amended August 19, 2002 to include sequence identifiers, as indicated in the following page capture from the USPTO IFW:



Withdrawal of the objection to the specification stated in ¶[14] of the Office Action dated September 19, 2005 is requested.

The claims are directed to the elected invention.

The objection to claim 34 noted in ¶[16] of the Office Action dated September 19, 2005 is moot in view of the above amendments.

The objection to claim 62 noted in ¶[17] of the Office Action dated September 19, 2005 is moot in view of the above amendments.

The Section 112, second paragraph, rejection of claims 31-35, 37-38, 51-62 and 64-66 is moot in view of the above. The claims are submitted to be definite, especially in view of the sequence which was part of the original disclosure by incorporation of the reference disclosing the same, as noted above.

The Section 112, second paragraph, rejection of claims 35 and 57 is moot in view of the above. The claims are submitted to be definite. Claim 57 has been represented as new claim 79 in a form believed to be definite.

The Section 112, first paragraph "written description", rejection of claims 31-35, 37-38, 51-62 and 64-66 is moot in view of the above. The claims are submitted to be supported by an adequate written description. Consideration of the following in this regard is requested.

The description and claims define that the *Photinus pyralis* luciferase amino acid sequence of SEQ ID NO: 37 as the reference sequence against which the recombinant proteins can be compared. Claim 67, for example, defines a genus encompassing a recombinant protein which has luciferase activity, at least 90% similarity to the *Photinus pyralis* wild-type luciferase of SEQ ID NO: 37, at least one mutation corresponding to residues 214, 232, 295, 14, 35 105, 234, 420 or 310 of the *Photinus pyralis* luciferase, and increased thermostability compared to the *Photinus pyralis* wild-type luciferase. Representative examples within the scope of the claimed genus are described in the specification, including recombinant proteins with the following mutations compared to the wild-type *Photinus pyralis* luciferase (of SEQ ID NO: 37): I232A/E354K, T214A/I232A/E354K, A215L/I232A/E354K, T214A/I232A/E354K/A215L, I232A/E354K/T214A/F295L, I232A/E354K/T214A F295L/F14A/L35A, I232A/E354K/T214A/F295L/F14A/L35A/A215L, A105V, T214A, T214C, T214N, T295L, I232A, F14A, L35A, D234G, S420T, H310R (see page 14, line 28 to page 15, line 9). Other representative examples of recombinant proteins within the scope of claim 67 are described in Examples 2-4 and 7.

The applicants submit that one of ordinary skill in the art would be aware of wild-type luciferases and that the applicants provide various distinguishing identifying characteristics of the claimed invention relating to structure (i.e. 90% similarity to the

luciferase of SEQ ID NO: 37) and biological function (i.e. luciferase function and increased thermostability) of recombinant proteins relating to the *Photinus pyralis* wild-type luciferase. Thus, the ordinarily skilled person with his background knowledge when reading the description and examples of the present application would appreciate that the applicants were in possession of the invention as claimed when the application was filed.

The applicants observe that, according to the USPTO "Revised Interim Written Description Guidelines Training Materials" available on the USPTO website, the "disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus" (page 31). The Examiner's attention is drawn in particular to Example 14 of the Training Materials, in which the exemplar claim is directed to a protein having a specific sequence and variants thereof with at least 95% identity to that sequence and capable of catalysing a specific biological reaction. The example provides that there is reduction to practice of the single disclosed species but that the claimed variants are contemplated but not exemplified. Yet the applicant is deemed to be in possession of the invention because the single species is representative of the claimed genus, all members of the genus must have a given structural identity to the given sequence, and there is an assay which would identify all of the claimed variants. By analogy with Example 14, the applicants submit that the present specification similarly provides an adequate written description, from which one of ordinary skill in the art would conclude that the applicants were in possession of the invention recited in the claims.

The applicants note that the term "similarity" is recited in the claims, which one of ordinary skill in the art will appreciate from the specification refers to a quantifiable parameter which involves measurement of sequence similarity between a recombinant protein and the wild-type luciferase of SEQ ID NO: 37 referred to in the claims. In the present application at page 13, lines 9 - 24, it is stated that sequence similarity may in particular be assessed (i.e. quantified) using the well-known Lipman and Pearson (1985) multiple alignment method, and the exact parameters which should be used in determination of similarity are provided. An ordinarily skilled person comparing an "unknown" sequence with the reference sequence of SEQ ID NO: 37 would, using the Lipman and Pearson method referred to in the application, arrive at only one value of sequence similarity and be able to determine whether or not the unknown sequence fell with the scope of the claims.

The Section 112, first paragraph "enablement", rejection of claims 31-35, 37-38, 51-62 and 64-66 is moot in view of the above. The claims are submitted to be supported by an enabling disclosure and consideration of the following in this regard is requested.

The applicants note that independent claim 67 covers recombinant proteins with luciferase activity, increased thermostability and at least 90% similarity compared to wild-type *Photinus pyralis* luciferase of SEQ ID NO: 37. As mentioned above, numerous representative examples within the scope of the claims are provided in the specification, and the applicants also provide clear teaching and guidance on how to make, test and use other species of recombinant proteins within the scope of the claims. The applicants submit that the amended claims are enabled for the reasons set out below.

The Examiner has referred to MPEP 2164.03 regarding predictability. However, in assessing enablement, MPEP 2164.01(a) also notes that the Examiner should consider several factors, including the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The Manual states that it is improper to conclude that a disclosure is not enabling based in an analysis of only one of the above factors while ignoring one or more of the others. The Examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. This has been reinforced by the recent decision of Capon v. Eshhar v. Dudas (US Court of Appeals for the Federal Circuit, 12 August 2005), where the court stated that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.

The applicants request that the Examiner takes into account all of the relevant factors regarding enablement and to not, for example, focus on only the aspect of predictability. Inventions in the biological sciences, for instance relating to recombinant proteins, may contain an amount of some unpredictability however if the same were an absolute bar to patentability, then it may not be possible for an applicant or patentee to claim a variant of a specific protein sequence by sequence identity or similarity

variation. This would be contrary to the Patent Office practice, as evidenced by previously granted U.S. patent claims and the Training Materials of the USPTO (see for example, Example 14 of the USPTO "Revised Interim Written Description Guidelines Training Materials" mentioned above). With sufficient teaching in the specification on how to make and test variants, as has been provided in the present application, there is no undue experimentation required by one of ordinary skill to make and use the full scope of the claimed invention. The applicants therefore respectfully submit that the application, as directed to one of ordinary skill and taking into account the state of the prior art, provides enablement for the claimed invention.

The Section 102 rejection of claims 31-32, 34-35, 37, 51-52, 60-62 and 64-65 over Database EMBL Accession Number D25415 "as evidenced by Wood et al. (US Patent Application Publication 2003/0068801)", is moot in view of the above. The Section 102 rejection of claims 31-32, 34-35, 37, 51-54, 57-62 and 64-66 over Wood is moot in view of the above. The Section 103 rejection of claims 55-56 over Firoozabady (U.S. Patent No. 5,480,789) in view of Wood is moot in view of the above. The claims are submitted to be patentable over the cited art and consideration of the following in this regard is requested.

With respect to the Examiner's reliance on EMBL Accession No. D25415 as evidenced by Wood et al. (US 2003/0068801), the applicants note that Wood et al. state in paragraph [0011] that their lucppe2 cDNA encodes a *Photuris pennsylvanica* firefly luciferase, LucPpe2, having a T249M mutation compared to wild-type *Photuris pennsylvanica* firefly luciferase and increased thermostability compared to wild-type *Photinus pyralis* luciferase. The Examiner appears to acknowledge that the sequences

of Wood et al. are not wild-type but mutant *Photuris pennsylvanica* firefly luciferases (see page 13 of the Office Action dated September 19, 2005). The EMBL Accession No. D25415 provides a wild-type *Photuris pennsylvanica* firefly luciferase. Wood et al. therefore does not provide evidence, as contended by the Examiner, that the wild-type *Photuris pennsylvanica* firefly luciferase of D25415 has increased thermostability compared to wild-type *Photinus pyralis* luciferase.

Furthermore, the applicants note that both the wild-type *Photuris pennsylvanica* firefly luciferase of D25415 as well as Wood et al.'s LucPpe2 and other mutants are not within the scope of the present claims. For example, LucPpe2 has only 88.7% similarity to the *Photinus pyralis* luciferase of SEQ ID NO: 37, as determined using the Lipman and Pearson (1985) alignment method with the parameters provided on page 13, lines 9 – 24 of the present application.

With respect to the Examiner's reliance on Wood et al., the applicants note, as mentioned above, that the *Photuris pennsylvanica* firefly luciferase mutants disclosed in Wood et al. do not fall within the scope of the present claims. In particular, the Wood et al. luciferase polypeptides of SEQ ID NO: 27-28, 30 and 32-33 have less than 90% similarity to the *Photinus pyralis* luciferase of SEQ ID NO: 37, as determined using the Lipman and Pearson (1985) alignment method with the parameters provided on page 13, lines 9 – 24 of the present application.

With respect to the Examiner's reliance on Firoozabady et al. (USP5,480,789) in view of Wood et al., the applicants note that Firoozabady et al. discloses a method for producing a somatic rose embryo (claim 1) which expresses an exogenous luciferase gene (claim 13). The method of claim 1 can be used to produce transformed plantlets (see

claim 2). However, Firoozabady et al. provides no suggestion or teaching that the exogenous luciferase gene could be a thermostable luciferase. Indeed, the purpose of the luciferase gene in Firoozabady et al. is to act as a reporter gene to facilitate screening of transformed callus and plant material (see column 5, lines 25-31). Neither does Wood et al. suggest or teach that their thermostable luciferases might be used as reporter genes in plant cells or in a plant. Therefore, there was no motivation to combine the teachings of Firoozabady et al. and Wood et al. to produce a plant cell or plant transformed with a thermostable luciferase.

Furthermore, even if the teachings of Firoozabady et al. and Wood et al. were to have been combined, one of ordinary skill would not have arrived at the presently claimed invention because the thermostable luciferases of the present invention are distinct from those in Wood et al., as explained above.

The Examiner is requested to hold in abeyance the obviousness-type double patenting rejection of claims 1-5, 7-8 and 21-23 over claims 1-4, 6-10, 14, 17-19 and "6-23" of copending application No. 10/111,723, until such time as allowable claims are identified

The claims are submitted to be patentable and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

SQUIRRELL et al.
Appl. No. 09/763,824
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Respectfully submitted,

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